The Toxic Environment and the Epigenetics of Fetal Growth

Principal Investigator: Burris, Heather Herson	
Institute Receiving Award	
Location	Boston, MA
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DESCRIPTION (provided by applicant):	: This application for a K23 Mentored Patient-Oriented Research Career Development Award includes a 5-year plan for training and research activities that will provide the skills and experience needed to achieve success as an independent investigator studying the role of the environment and epigenetic mechanisms in birth outcomes. The candidate has completed research and clinical fellowships that prepared her for an academic career studying perinatal social epidemiology and is currently a full-time faculty member in the Department of Neonatology at Beth Israel Deaconess Medical Center. The candidate is a core member of the Division of Newborn Medicine at Harvard Medical School serving as an Instructor in pediatrics, which is the standard entry level academic position at Harvard. This K23 award will provide her with the structure and support necessary to accomplish the following goals: (1) assess the role that arsenic plays in fetal growth; (2) assess the role arsenic plays in the DNA methylation of genes involved in fetal growth such as inflammatory cytokine genes and the glucocorticoid receptor gene, and explore whether arsenic affects fetal growth through such epigenetic mechanisms; (3) gain expertise in environmental toxicology and environmental epigenetic analyses; and (4) learn the administrative skills needed to manage a large cohort study so that transition to an independent research career running her own birth cohort is accomplished. The candidate's goal is to examine the role the toxic chemical environment plays in birth outcome disparities in the US. To achieve these goals, Dr. Burris has assembled a mentoring team comprised of a primary mentor, Robert Wright, MD MPH, Associate Professor of Pediatrics and Environmental Health who is an expert in pediatric environmental health and toxicology, and co-mentor Andrea Baccarelli, MD PhD, the Mark and Catherine Winkler Associate Professor of Environmental Epigenetics, who has expertise in epigenetic analyses. Although chemicals like arsenic are known to affect birth outcomes and known to affect DNA methylation, it remains unknown whether DNA methylation mediates arsenic-birth weight associations. The study proposed is designed to test the hypothesis that arsenic impairs fetal growth, that arsenic causes alterations in the DNA methylation of inflammatory cytokine genes and the glucocorticoid receptor gene. The candidate will explore whether DNA methylation disturbances mediate arsenic-birth weight associations. These analyses will be performed within a previously established, currently funded cohort in Mexico City

	(ELEMENT) directed by Dr. Wright. The candidate will use the abundant resources available at Beth Israel Deaconess Medical Center, the Harvard Catalyst (Clinical and Translational Science Center) and the Harvard School of Public Health to obtain the training and coursework necessary to supplement the practical training attained through these analyses to become an independent investigator with a research program studying the environmental impact on birth outcome disparities. Public Health Relevance: Poor fetal growth is associated with short-term perinatal morbidity and mortality as well as long-term poor health later in life. Arsenic exposure during pregnancy has been shown to potentially inhibit fetal growth in animals and to be associated with low birth weights in humans. Understanding the biology of arsenic toxicity and its effect on fetal growth may ultimately spurn tighter environmental regulation policies, trigger clean-up efforts and allow for targeted therapies during pregnancies affected by high arsenic exposure.
Science Code(s)/Area of Science(s)	Primary: 10 - Epigenetics
Publications	See publications associated with this Grant.
Program Administrator	Carol Shreffler (shreffl1@niehs.nih.gov)